

Beg 55,72,154,399,351

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File 55:BIOSIS PREVIEWS(R) 1985-1996/Sep W3

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2/7/1 (Item 1 from file: 55)

DIALOG(R) File 55:BIOSIS PREVIEWS(R)

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11473588 BIOSIS Number: 98073588

Localization of ligands for L-selectin in mouse peripheral lymph node
high endothelial cells by colloidal gold conjugates

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Blood 84 (11). 1994. 3766-3775.

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L-selectin, a Ca-2+-dependent lectin-like receptor, mediates lymphocyte attachment to high endothelial venules (HEV) of peripheral lymph nodes (PLN) during the process of lymphocyte homing. Two endothelial-derived ligands for L-selectin, known as GlyCAM-1 (Sgp50) and CD34 (Sgp90), have

7.23, 7.24 [IMAGE AVAILABLE]

6. 5,548,065, Aug. 20, 1996, Tyrosine kinase receptor human flk-2-specific antibodies; Ihor R. Lemischka, 530/388.22, 387.9, 388.23, 388.7, 389.2, 389.6 [IMAGE AVAILABLE]

7. 5,543,328, Aug. 6, 1996, Adenoviruses having modified fiber proteins; Alan McClelland, et al., 435/320.1; 424/93.1, 93.2; 536/23.4, 23.72; 935/22, 32, 57 [IMAGE AVAILABLE]

8. 5,543,312, Aug. 6, 1996, *Pastuerella haemolytica* glycoprotease gene and the purified enzyme; Alan Mellors, et al., 435/220, 240.2, 252.3, 320.1; 536/23.2, 24.32 [IMAGE AVAILABLE]

9. 5,541,103, Jul. 30, 1996, **CD34**+ peripheral blood progenitor cells obtained by ex vivo expansion; Lothar Kanz, et al., 435/240.2; 424/85.1, 93.71; 435/240.25 [IMAGE AVAILABLE]

10. 5,541,072, Jul. 30, 1996, Method for magnetic separation featuring magnetic particles in a multi-phase system; Yuzhou Wang, et al., 435/7.21; 209/214, 223.1; 210/222, 695, 767; 435/2, 5, 6, 7.1, 7.23, 7.31, 7.32; 436/177, 501, 518, 526, 807, 824 [IMAGE AVAILABLE]

11. 5,536,641, Jul. 16, 1996, Monoclonal antibody specific for vascular endothelial cell antigen endoglyx-1 and uses thereof for detection of, and isolation of, vascular endothelial cells; Maria P. Sanz-Moncasi, et al., 435/7.21, 7.23, 70.21, 172.2, 240.27, 261; 530/388.2, 388.22 [IMAGE AVAILABLE]

12. 5,536,475, Jul. 16, 1996, Apparatus for magnetic cell separation; Ahmad-Maher Moubayed, et al., 422/101; 209/217, 225, 232; 210/222; 422/44, 99; 435/2, 7.21, 962, 971; 436/526, 806, 807; 604/6 [IMAGE AVAILABLE]

13. 5,530,101, Jun. 25, 1996, Humanized immunoglobulins; Cary L. Queen, et al., 530/387.3; 424/133.1, 143.1; 530/387.1, 388.22 [IMAGE AVAILABLE]

14. 5,523,286, Jun. 4, 1996, Stroma-derived proteoglycan containing composition which promotes differentiation and maintains the self-renewal capacity of long-term bone marrow culture-initiating cells; Philip B. McGlave, et al., 514/8; 435/240.2, 240.21, 240.3; 514/21; 536/20, 21 [IMAGE AVAILABLE]

15. 5,521,067, May 28, 1996, Bone marrow cell adhesion molecules and process for detecting adherence between cell adhesion molecules and cells generally; Beerelli Seshi, 435/7.24, 7.2, 7.9, 29, 961, 962; 436/63, 516 [IMAGE AVAILABLE]

16. 5,519,028, May 21, 1996, Antiviral preparations; Mirko Beljanski, 514/285, 307 [IMAGE AVAILABLE]

17. 5,514,340, May 7, 1996, Device for separating magnetically labelled cells; Peter Lansdorp, et al., 422/101; 209/223.1, 223.2, 636; 210/222, 695; 422/99; 435/2, 7.23; 436/526 [IMAGE AVAILABLE]

18. 5,512,480, Apr. 30, 1996, Flow-through bioreactor with grooves for cell retention; Craig Sandstrom, et al., 435/289.1; 220/670; 435/293.1, 299.1, 304.2, 813 [IMAGE AVAILABLE]

19. 5,512,442, Apr. 30, 1996, Detection of vascular adhesion protein-1 (VAP-1); Sirpa Jalkanen, et al., 435/7.21, 7.1, 7.2 [IMAGE AVAILABLE]
20. 5,506,126, Apr. 9, 1996, Rapid immunoselection cloning method; Brian Seed, et al., 435/172.3, 320.1; 536/24.2 [IMAGE AVAILABLE]
21. 5,498,599, Mar. 12, 1996, Methods for stimulating platelet production; Esther S. Choi, et al., 514/12, 2, 814, 833, 885 [IMAGE AVAILABLE]
22. 5,489,578, Feb. 6, 1996, Sulfated ligands for l-selectin and methods of treating inflammation; Steven D. Rosen, et al., 514/61, 25, 53, 54, 62; 536/4.1, 17.2, 18.7, 53, 54, 55, 55.1, 55.2 [IMAGE AVAILABLE]
23. 5,489,516, Feb. 6, 1996, Hybridoma and monoclonal antibody specific for human stem cell factor receptor and methods of use of the monoclonal antibody for detection of stem cell factor receptors; Virginia C. Broudy, et al., 435/7.23, 7.21, 7.24, 172.2, 240.27; 530/387.7, 388.22, 388.23 [IMAGE AVAILABLE]
24. 5,486,536, Jan. 23, 1996, Sulfatides as anti-inflammatory compounds; Peter A. Ward, et al., 514/460 [IMAGE AVAILABLE]
25. 5,480,825, Jan. 2, 1996, AG-F human T cell line with unique phenotype and cytokine secretions; Yair Gazitt, 435/240.25, 240.1, 240.2 [IMAGE AVAILABLE]
26. 5,474,687, Dec. 12, 1995, Methods for enriching **CD34**.sup.+ human hematopoietic progenitor cells; Peter Van Vlasselaer, 210/782; 422/72, 102; 435/2; 494/16; 604/49, 187, 191 [IMAGE AVAILABLE]
27. 5,472,867, Dec. 5, 1995, Ex vivo expansion of peripheral blood progenitor cells; Lothar Kanz, et al., 435/240.25; 424/85.1, 85.2, 85.5, 93.71, 144.1; 435/240.3 [IMAGE AVAILABLE]
28. 5,468,612, Nov. 21, 1995, 9804 gene and methods of use thereof; Edward H. Cohen, et al., 435/6, 240.2, 320.1; 536/23.5; 935/1, 22, 24, 76, 77, 78 [IMAGE AVAILABLE]
29. 5,466,572, Nov. 14, 1995, High speed flow cytometric separation of viable cells; Dennis T. Sasaki, et al., 435/2; 436/63, 172 [IMAGE AVAILABLE]
30. 5,464,753, Nov. 7, 1995, Purification and manipulation of bone marrow and blood cells on the basis of P-glycoprotein expression; Preet M. Chaudhary, et al., 435/7.24, 2, 7.21, 240.2; 436/56, 172, 536 [IMAGE AVAILABLE]
31. 5,460,964, Oct. 24, 1995, Method for culturing hematopoietic cells; Philip B. McGlave, et al., 435/240.21, 240.1, 240.2, 240.241, 240.25 [IMAGE AVAILABLE]
32. 5,459,069, Oct. 17, 1995, Device for maintaining and growing human stem and/or hematopoietics cells; Bernhard O. Palsson, et al., 435/289.1, 293.1, 293.2, 297.1, 297.2 [IMAGE AVAILABLE]
33. 5,439,586, Aug. 8, 1995, Magnetic filter with ordered wire array;

Adrian J. Richards, et al., 210/222, 456 [IMAGE AVAILABLE]

34. 5,436,151, Jul. 25, 1995, Method for culturing human hematopoietic stem cells in vitro; Philip B. McGlave, et al., 435/240.1, 240.2, 240.21, 240.241, 240.25 [IMAGE AVAILABLE]

35. 5,429,927, Jul. 4, 1995, Antigen/anti-antigen cleavage; John Afseth, et al., 435/7.2, 2, 7.24, 239, 240.2, 243, 261, 975; 436/512, 518, 526; 530/391.1 [IMAGE AVAILABLE]

36. 5,418,129, May 23, 1995, Blood treatment method; Edward Nudelman, et al., 435/2; 424/140.1; 435/70.21, 240.27; 530/388.23, 388.25 [IMAGE AVAILABLE]

37. 5,409,826, Apr. 25, 1995, Preserved, non-infectious control cells prepared by the modulation or modification of normal cells; John A. Maples, et al., 435/240.2, 2, 29; 436/10; 536/124 [IMAGE AVAILABLE]

38. 5,409,825, Apr. 25, 1995, Expansion of human hematopoietic progenitor cells in a liquid medium; Ronald Hoffman, et al., 435/240.1, 240.2, 240.21, 240.25 [IMAGE AVAILABLE]

39. 5,409,813, Apr. 25, 1995, Method for mammalian cell separation from a mixture of cell populations; Richard M. Schwartz, 435/7.24; 210/660, 661, 695; 435/2, 30, 240.2; 436/526 [IMAGE AVAILABLE]

40. 5,378,624, Jan. 3, 1995, Methods for removing ligands from a particle surface; Ronald J. Berenson, et al., 435/239, 240.21, 243, 254.1, 261; 436/541, 824, 828 [IMAGE AVAILABLE]

41. 5,374,531, Dec. 20, 1994, Immunoassay for determination of cells; Bruce D. Jensen, 435/7.24, 7.32, 7.92, 975; 436/518, 523, 526, 533, 534 [IMAGE AVAILABLE]

42. 5,369,009, Nov. 29, 1994, Antibodies for P-glycoprotein encoded by the mdr1 gene and uses thereof; Robert J. Arceci, et al., 424/1.49; 435/7.21, 7.23, 240.27, 243; 530/387.7, 388.8 [IMAGE AVAILABLE]

43. 5,367,057, Nov. 22, 1994, Tyrosine kinase receptor flk-2 and fragments thereof; Ihor R. Lemischka, 530/350, 403 [IMAGE AVAILABLE]

44. 5,362,631, Nov. 8, 1994, C-myb transfected T98G cells which produce GM-CSF and stem cell factor; Bruno Calabretta, 435/69.5, 69.4, 240.2 [IMAGE AVAILABLE]

45. 5,359,046, Oct. 25, 1994, Chimeric chains for receptor-associated signal transduction pathways; Daniel J. Capon, et al., 536/23.4; 435/6, 69.1, 70.2, 235.1, 240.1, 240.2, 320.1; 530/350; 536/23.1, 23.5, 23.51, 23.52, 23.53 [IMAGE AVAILABLE]

46. 5,356,373, Oct. 18, 1994, Method and apparatus for autologous transfusions in premature infants; Robert A. Dracker, 604/4, 317 [IMAGE AVAILABLE]

47. 5,348,859, Sep. 20, 1994, Method and apparatus for obtaining an absolute white blood cell subset count and white blood cell multipart differential; Robert F. Brunhouse, et al., 435/7.24, 7.2, 7.21, 7.23

[IMAGE AVAILABLE]

48. 5,340,719, Aug. 23, 1994, Method and apparatus for optically screening microscopic cells; Constance M. Hajek, et al., 435/7.21, 7.2, 7.23, 7.24 [IMAGE AVAILABLE]

49. 5,322,787, Jun. 21, 1994, Cytokine and bioassay therefor; Michael Martin, et al., 435/240.2, 29, 240.1 [IMAGE AVAILABLE]

50. 5,283,354, Feb. 1, 1994, Nucleic acids encoding hematopoietic stem cells receptors flk-1; Ihor R. Lemischka, 536/23.5; 435/69.1; 530/350, 403 [IMAGE AVAILABLE]

51. 5,270,458, Dec. 14, 1993, Nucleic acids encoding fragments of hematopoietic stem cell receptor flk-2; Ihor R. Lemischka, 536/23.5; 435/69.1, 320.1; 530/350, 403 [IMAGE AVAILABLE]

52. 5,256,534, Oct. 26, 1993, CD4.sup.+, latently HIV-1-infected hematopoietic progenitor cells; Salvatore T. Butera, et al., 435/5, 7.24, 8, 239, 240.26 [IMAGE AVAILABLE]

53. 5,252,479, Oct. 12, 1993, Safe vector for gene therapy; Arun Srivastava, 435/235.1, 240.2, 320.1 [IMAGE AVAILABLE]

54. 5,246,699, Sep. 21, 1993, Maturation of hemopoietic cells; Patrice Debre, et al., 424/85.2; 435/975; 514/8, 12, 21; 530/351 [IMAGE AVAILABLE]

55. 5,234,816, Aug. 10, 1993, Method for the classification and monitoring of leukemias; Leon W. M. M. Terstappen, 435/7.24; 436/64, 172, 536 [IMAGE AVAILABLE]

56. 5,206,345, Apr. 27, 1993, IL-4 and TNF induce mAb 6G10-recognized expression on bone marrow stromal cells; Boris Masinovsky, et al., 530/388.7; 435/7.21, 240.27; 436/548 [IMAGE AVAILABLE]

57. 5,199,942, Apr. 6, 1993, Method for improving autologous transplantation; Steven Gillis, 604/4; 128/898; 424/85.2, 529; 435/240.21; 604/49 [IMAGE AVAILABLE]

58. 5,198,356, Mar. 30, 1993, Monophenotypic in vitro cell lines of megakaryocytic lineage, products produced thereby and methods; Michael A. Lieberman, et al., 435/240.2, 240.1, 240.23 [IMAGE AVAILABLE]

59. 5,185,438, Feb. 9, 1993, Nucleic acids encoding hematopoietic stem cell receptor flk-2; Ihor R. Lemischka, 536/23.2; 435/69.1, 320.1; 530/350, 403 [IMAGE AVAILABLE]

60. 5,147,784, Sep. 15, 1992, T-lymphocyte progenitor cell assay; Bruno Peault, 435/7.24, 30, 34, 240.2, 243 [IMAGE AVAILABLE]

61. 5,137,809, Aug. 11, 1992, Method to determine the composition of bone marrow samples; Michael R. Loken, et al., 435/7.21; 422/61; 435/7.1, 7.2; 436/546, 800 [IMAGE AVAILABLE]

62. 5,128,259, Jul. 7, 1992, Factor-dependent hematopoietic cell line exhibiting epo-induced erythrocyte maturation; Doris A. Morgan, 435/240.2, 240.1, 240.25, 948 [IMAGE AVAILABLE]

63. 5,081,030, Jan. 14, 1992, Release of cells from affinity matrices;
Curt I. Civin, 435/240.2; 424/577; 435/2, 240.23, 267 [IMAGE AVAILABLE]

64. 5,061,620, Oct. 29, 1991, Human hematopoietic stem cell; Ann
Tsukamoto, et al., 435/7.21, 240.2, 240.21 [IMAGE AVAILABLE]

65. 5,041,289, Aug. 20, 1991, Method of purging residual tumor cells in
vitro with lymphokine activated cytotoxic cells; Joseph H. Phillips, et
al., 424/85.2, 85.1, 85.4, 93.7, 93.71, 93.73, 534, 573, 577, 578;
435/240.1, 240.2, 240.21 [IMAGE AVAILABLE]

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been identified by affinity precipitation of lymph nodes extracts with a chimeric molecule that combines the extracellular domains of L-selectin with the human IgG1 Fc region (L-selectin-IgG) (J Cell Biol 110:2221, 1990). Here, using a histologic probe based on colloidal gold conjugated to L-selectin-IgG (LS-Ig), we performed morphologic mapping of the HEV ligands in PLN at both the light and electron microscopic levels. With a postembedding labeling method, intense LS-Ig-gold staining of PLN HEV was observed, while the HEV of Peyer's patches (PP) were negative. The specificity of LS-Ig-gold staining was established by pretreatment of sections with sialidase and coincubation of sections with EGTA, fucoidin, or L-selectin-IgG itself. In ultrastructural studies of high endothelial cells(HEC), gold particles were bound to the trans-Golgi network(TGN) and to peripheral vesicles in the cytoplasm. Gold labeling was also detected in a patchy distribution on the entire luminal vascular surface of HEC. Although the perivascular fibroreticular sheath of HEV was frequently labeled, limited labeling was observed on the basolateral surfaces of the HEC. In most cases, the HEC membrane surrounding migrating lymphocytes was negative. These results show that L-selectin ligands pass through the Golgi apparatus during their biosynthesis, are stored in secretory granules, and are expressed on the vascular luminal surface of the HEC. A polyclonal antiserum to GlyCAM-1 intensely stained intracellular organelles in the biosynthetic pathway including cytoplasmic vesicles, but failed to stain the cell surface of HEC. Given its presence in serum as a soluble factor, GlyCAM-1 is likely to be a secretory product.

2/7/2 (Item 2 from file: 55)
DIALOG(R) File 55:BIOSIS PREVIEWS(R)
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11445757 BIOSIS Number: 98045757

Sulfation-dependent recognition of high endothelial venules (HEV)-ligands by L-selection and MECA 79, an adhesion-blocking monoclonal antibody

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Journal of Experimental Medicine 180 (6). 1994. 2219-2226.

Full Journal Title: Journal of Experimental Medicine

ISSN: 0022-1007

Language: ENGLISH

Print Number: Biological Abstracts Vol. 099 Iss. 003 Ref. 030301

L-selectin is a lectin-like receptor that mediates the attachment of lymphocytes to high endothelial venules (HEV) of lymph nodes during the process of lymphocyte recirculation. Two sulfated, mucin-like glycoproteins known as Sgp50/GlyCAM-1 and Sgp90/CD34 have previously been identified as HEV-associated ligands for L-selectin. These proteins were originally detected with an L-selectin/Ig chimera called LEC-IgG. GlyCAM-1 and CD34 are also recognized by an antiperipheral node addressin (PNAd) mAb called MECA 79, which blocks L-selectin-dependent adhesion and selectively stains lymph node HEV. The present study compares the requirements for the binding of MECA 79 and LEC-IgG to HEV-ligands. Whereas desialylation of GlyCAM-1 and CD34 drastically reduced binding to LEC-IgG, this treatment enhanced the binding of GlyCAM-1 to MECA 79. In contrast, the binding of both MECA 79 and LEC-IgG to GlyCAM-1 and CD34 was greatly decreased when the sulfation of these ligands was reduced with chlorate, a metabolic inhibitor of sulfation. Because MECA 79 stains HEV-like vessels at various sites of inflammation, recognition by L-selectin of ligands outside of secondary lymphoid organs may depend on sulfation. In addition to their reactivity with GlyCAM-1 and CD34, both MECA 79 and LEC-IgG recognize an independent

molecule of apprx 200 kD in a sulfate-dependent manner. Thus, this molecule, which we designate Sgp200, is an additional ligand for L-selectin.

2/7/3 (Item 3 from file: 55)
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10801195 BIOSIS Number: 97001195
Binding of L-selectin to the vascular sialomucin CD34
Baumheuter S; Singer M S; Henzel W; Hemmerich S; Renz M; Rosen S D; Lasky
L A
Dep. Immunol., Genentech Inc., South San Francisco, CA 94080, USA
Science (Washington D C) 262 (5132). 1993. 436-438.
Full Journal Title: Science (Washington D C)
ISSN: 0036-8075
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 001 Ref. 001138
The adhesive interactions between leukocyte L-selectin and the endothelium are involved in the migration of lymphocytes through peripheral lymph nodes and of neutrophils to sites of inflammation. A recombinant L-selectin stains high endothelial venules (HEVs) in lymph nodes and recognizes sulfated carbohydrates found on two endothelial glycoproteins, Sgp50 and Sgp90. Amino acid sequencing of purified Sgp90 revealed a protein core identical to that of CD34, a sialomucin expressed on hematopoietic stem cells and endothelium. A polyclonal antiserum to recombinant murine CD34 stains peripheral lymph node endothelium and recognizes Sgp90 that is functionally bound by L-selectin. Thus, an HEV glycoform of CD34 can function as a ligand for L-selectin.

2/7/4 (Item 4 from file: 55)
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10801155 BIOSIS Number: 97001155
L-selectin and its biological ligands
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94143-0452, USA

Histochemistry 100 (3). 1993. 185-191.
Full Journal Title: Histochemistry
ISSN: 0301-5564
Language: ENGLISH

Print Number: Biological Abstracts Vol. 097 Iss. 001 Ref. 001108

This review considers the leukocyte adhesive receptor known as L-selectin. This protein, belonging to the selectin family of cell-cell adhesion receptors, mediates adhesion by virtue of a C-type lectin domain at its amino terminus. The protein was discovered as a lymphocyte homing receptor involved in the attachment of lymphocytes to high endothelial venules (HEV) of lymph nodes. Its widespread distribution on all leukocyte populations underlies a more general role in a variety of leukocyte-endothelial interactions. In the HEV interaction, cognate HEV ligands for L-selectin have been identified as two sulfated, sialylated, and fucosylated glycoproteins, known as GlyCAM-1 and Sgp90. These ligands have mucin-like domains which confer important properties for their proposed adhesive function. The carbohydrate features of these ligands,

essential for their interaction with L-selectin, are reviewed. The existence of extra-lymphoid ligands for L-selectin is also discussed.

2/7/5 (Item 5 from file: 55)
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10104576 BIOSIS Number: 95104576
SULPHATION REQUIREMENT FOR GLYCAMS-1 AN ENDOTHELIAL LIGAND FOR L SELECTIN
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NATURE (LOND) 361 (6412). 1993. 555-557. CODEN: NATUA
Full Journal Title: NATURE (London)
Language: ENGLISH

L-selectin participates in the initial attachment of leukocytes to the vascular endothelium¹⁻³. On lymphocytes, it mediates binding to high endothelial venules of lymph nodes. As a selectin⁴⁻⁶ it functions as a calcium-dependent lectin^{7,8} recognizing carbohydrate-bearing ligands on endothelial cells⁹⁻¹¹. Two lymph node ligands for L-selectin have been identified as sulphated glycoproteins of Mr .apprx.50K and .apprx.90K, called Sgp50 and Sgp90 (ref. 10). The recently cloned Sgp50 (ref.12), now designated GlyCAM-1, is a high endothelial venule-associated, mucin-like glycoprotein containing predominantly O-linked carbohydrate chains. Sialylation of GlyCAM-1 is necessary for its ligand activity^{9,10,13} and a role for fucosylation is suspected¹³. We have used chlorate as a metabolic inhibitor of sulphation, and report here that GlyCAM-1 has an additional requirement for sulphate.

2/7/6 (Item 6 from file: 55)
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9599143 BIOSIS Number: 94104143
FURTHER CHARACTERIZATION OF THE INTERACTION BETWEEN L SELECTIN AND ITS
ENDOTHELIAL LIGANDS

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94143-0452.

GLYCOBIOLOGY 2 (4). 1992. 373-381. CODEN: GLYCE
Language: ENGLISH

L-selectin is a lectin-like receptor on lymphocytes which mediates their attachment to high endothelial venules (HEV) within lymph nodes. Previous work has identified HEV-associated endothelial ligands for L-selectin as sialylated, fucosylated and sulphated glycoproteins of .apprx.50 kDa and .apprx.90 kDa (Sgp50 and Sgp90). The interaction of L-selectin with these ligands is carbohydrate directed, reflecting the involvement of its amino-terminal, calcium-type lectin domain. It has been reported, and we have confirmed, that anti-Ly22 blocks the adhesive function of L-selectin without reducing its binding to a carbohydrate-based ligand PPME (phosphomannan monoester core from *Hansenula hostii*). The epitope for this monoclonal antibody depends on the epidermal growth factor (EGF) domain of L-selectin. We demonstrate that anti-Ly22 inhibits the interaction of L-selectin with both of the Sgps, thus establishing that the interaction of L-selectin with HEV can be accounted for by the Sgps. Furthermore, the interaction of trypsin fragments of Sgp50 with L-selectin is inhibitible

both by an antibody that maps to the lectin domain and by anti-Ly22. These findings raise the possibility that anti-Ly22 is affecting the function of the lectin domain of L-selectin rather than directly antagonizing the EGF domain. Toward a further characterization of L-selectin's carbohydrate specificity, we show that Sgp50 is partially inactivated by the linkage specific Newcastle Disease virus sialidase (.alpha.2,3 linkage). We additionally demonstrate that a sialyl Lewis x-related tetrasaccharide can interact with L-selectin, as has also been demonstrated for E-selectin and P-selectin.

2/7/7 (Item 7 from file: 55)
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9082149 BIOSIS Number: 93067149

TUMOR-ANTIGEN-SPECIFIC HUMORAL IMMUNE RESPONSE OF ANIMALS TO
ANTI-IDIOTYPIC ANTIBODIES AND COMPARATIVE SEROLOGICAL ANALYSIS OF PATIENTS
WITH SMALL-CELL LUNG CARCINOMA

LEHMANN H-P; ZWICKY C; WAIBEL R; STAHEL R A

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INT J CANCER 50 (1). 1992. 86-92. CODEN: IJCNA

Full Journal Title: International Journal of Cancer

Language: ENGLISH

We have previously developed 3 monoclonal anti-idiotypic antibodies (Ab2) of LOU rat origin directed against the binding site of the murine monoclonal IgM LAM8, which recognizes the small-cell lung carcinoma (SCLC)-associated sialoglycoprotein antigen SGP90-135. The aim of this study was to compare the efficiencies of these 3 Ab2, designated LY8-229, LX8-531 and LX8-632, to induce antigen-specific immunity in different animal species without prior exposure of the recipients to the nominal antigen, and thereby possibly select an Ab2 candidate for active immunotherapy against SCLC in patients. The feasibility of this approach was further evaluated by a serological analysis of patients with SCLC compared with healthy individuals, of patients with SCLC compared with healthy individuals, in whom the spontaneous antibody reactivities against SCLC cell lines and Ab2 were tested. LY8-229 was shown to be the most effective AB2 in inducing antigen-specific antibodies in BALB/c mice CBA/J/Zur mice and one NZW rabbit. Furthermore, LY8-229 was the only Ab2 against which significantly elevated idiotype-specific antibody reactivities existed in sera of patients with SCLC. These reactivities correlated positively with binding to antigen-positive tumor cells. Our findings suggest that LY8-229 represents in its reactivity pattern the nominal SCLC antigen in humans also, and therefore may be of diagnostic and possibly therapeutic relevance for patients with SCLC.

2/7/8 (Item 8 from file: 55)
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8561339 BIOSIS Number: 92026339

IDENTIFICATION OF A CARBOHYDRATE-BASED ENDOTHELIAL LIGAND FOR A
LYMPHOCYTE HOMING RECEPTOR

IMAI Y; SINGER M S; FENNIE C; LASKY L A; ROSEN S D

DEP. ANATOMY, PROGRAM IMMUNOL., UNIVERSITY CALIF., SAN FRANCISCO, CALIF.
94143-0452.

J CELL BIOL 113 (5). 1991. 1213-1222. CODEN: JCLBA

Full Journal Title: Journal of Cell Biology

Language: ENGLISH

Lymphocyte attachment to high endothelial venules within lymph nodes is mediated by the peripheral lymph node homing receptor (pnHR), originally defined on mouse lymphocytes by the MEL-14 mAb. The pnHR is a calcium-dependent lectin-like receptor, a member of the LEC-CAM family of adhesion proteins. Here, using a soluble recombinant form of the homing receptor, we have identified an endothelial ligand for the pnHR as an apprx. 50-kD sulfated, fucosylated, and sialylated glycoprotein, which we designate Sgp50 (sulfated glycoprotein of 50 kD). Recombinant receptor binding to this lymph node-specific glycoprotein requires calcium and is inhibitible by specific carbohydrates and by MEL-14 mAb. Sialylation of the component is required for binding. Additionally, the glycoprotein is precipitated by MECA-79, an adhesion-blocking mAb reaction with lymph node HEV. A related glycoprotein of apprx. 90 kD (designated as Sgp90) is also identified.

2/7/9 (Item 9 from file: 55)

DIALOG(R) File 55:BIOSIS PREVIEWS(R)

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7106093 BIOSIS Number: 88028838

MONOCLONAL ANTI-IDIOTYPIC ANTIBODY MIMICKING A TUMOR-ASSOCIATED
SIALOGLYCOPROTEIN ANTIGEN HUMORAL IMMUNE RESPONSE AGAINST HUMAN SMALL-CELL
LUNG CARCINOMA

BARTH A; WAIBEL R; STAHEL R A

DIV. ONCOL., UNIV. HOSP., CH-8091 ZURICH, SWITZ.

INT J CANCER 43 (5). 1989. 896-900. CODEN: IJCNA

Full Journal Title: International Journal of Cancer

Language: ENGLISH

We have previously described the tumor-associated sialglycoprotein antigen sGP90-135 defined by the murine LAM8 MAb. The antigen is characterized by strong membrane expression in a proportion of small-cell carcinomas of the lung, but little or no expression on normal tissues of epithelial or neural origin or on blood cells. With the aim of obtaining anti-idiotypic antibodies which might be useful as surrogates for sgp90-135 in vaccination studies, LOU rats were immunized with LAM8 MAb and their spleen cells fused with Y3 rat myeloma cells. The LY8-229 hybrid was selected by an anti-idiotype competition radioimmunoassay on antigen-positive target cells. LY8-229 was shown to be a rat IgG1 with high specificity for LAM8 combining site. Solubilized small-cell carcinoma extract, as well as antibody SEN I6, which recognizes the same tumor-associated antigen sGP90-135, selectively inhibited ¹²⁵I-LY8-229 binding to LAM8. Serum from BALB/c mice and DA rats immunized with anti-idiotypic antibody LY8-229 showed reactivity with antigen-positive target cell lines, but not with antigen-negative control cell lines. The induction of a specific immune response in 2 different species by the anti-idiotypic antibody LY8-229 suggests that LY8-229 bears the internal image of the antigen sGP90-135 and that it might be a candidate for immunotherapy trials in cancer patients.

2/7/10 (Item 10 from file: 55)

DIALOG(R) File 55:BIOSIS PREVIEWS(R)

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6605103 BIOSIS Number: 86071654

TUMOR-ASSOCIATED MEMBRANE SIALOGLYCOPROTEIN ON HUMAN SMALL CELL LUNG
CARCINOMA IDENTIFIED BY THE IgG2A MONOCLONAL ANTIBODY SWA20

WAIBEL R; O'HARA C J; SMITH A; STAHEL R A

DIV. ONCOL., UNIV. HOSP., CH-8091 ZURICH, SWITZ.

CANCER RES 48 (15). 1988. 4318-4323. CODEN: CNREA

Full Journal Title: Cancer Research

Language: ENGLISH

A mouse IgG2a monoclonal antibody, SWA20, defining a tumor-associated cell surface antigen on small cell carcinoma of the lung (SCC) was generated. The reactivity of the antibody with cell lines was examined by indirect immunofluorescence staining and solid phase radioimmunoassay and the reactivity with tissues by immunoperoxidase staining. The antibody reacts with a proportion of small cell carcinoma cell lines (4 of 8) and tissues (7 of 12), but not with other pulmonary or extrapulmonary cell lines (0 of 30) or tumor tissues (0 of 78). The antibody was unreactive with primary cultures of normal bronchial epithelial cells, RBC, and WBC. Immunoperoxidase staining of normal tissues showed rare antigen-positive cells in suprabasal layers of bronchial epithelium and less than 10% of positive cells in colon epithelium. Immunoblots of SCC extracts demonstrated antibody reactivity with a doublet band at Mr 40,000, a broader band at Mr 100,000, and a band at Mr 180,000. The antigen was not present in crude lipid extracts of SCC cells. Solid phase radioimmunoassays and immunoblots showed binding competition with the lectin Triticum vulgaris, sensitivity of the antigen to neuraminidase, and a partial sensitivity to treatment with periodate. The antigen was coexpressed on SCC cell lines with the antigen sGP90-135 defined first by antibody LAM8 (R. Waibel, C. J. O'Hara, and R. A. Stahel. Cancer Res., 47: 3766-3770, 1987) but differed from it by lack of reactivity with Lea-positive saliva and partial resistance to periodate treatment. There was no binding competition between radiolabeled antibodies SWA20 and LAM8 to SCC target cells. The IgG2a antibody SWA20 identifies a previously undescribed tumor-associated surface membrane antigen, sGP100, expressed selectively on a proportion of SCC.

2/7/11 (Item 1 from file: 72)

DIALOG(R) File 72:EMBASE

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9406303 EMBASE No: 94357259

Sulfation-dependent recognition of high endothelial venules (HEV)-ligands by L-selectin and MECA 79, an adhesion-blocking monoclonal antibody

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Department of Anatomy, University of California, San Francisco, CA
94143-0452 USA

J. EXP. MED. (USA) , 1994, 180/6 (2219-2226) CODEN: JEMEA ISSN:
0022-1007

LANGUAGES: English SUMMARY LANGUAGES: English

L-selectin is a lectin-like receptor that mediates the attachment of lymphocytes to high endothelial venules (HEV) of lymph nodes during the process of lymphocyte recirculation. Two sulfated, mucin-like glycoproteins known as Sgp50/GlyCAM-1 and Sgp90/CD34 have previously been identified as HEV-associated ligands for L-selectin. These proteins were originally detected with an L-selectin/Ig chimera called LEC-IgG. GlyCAM-1 and CD34 are also recognized by an anti-peripheral node addressin (PNAd) mAb called MECA 79, which blocks L-selectin-dependent adhesion and selectively stains lymph node HEV. The present study compares the requirements for the binding of MECA 79 and LEC-IgG to HEV-ligands. Whereas desialylation of GlyCAM-1

and CD34 drastically reduced binding to LEC-IgG, this treatment enhanced the binding of GlyCAM-1 to MECA 79. In contrast, the binding of both MECA 79 and LEC-IgG to GlyCAM-1 and CD34 was greatly decreased when the sulfation of these ligands was reduced with chlorate, a metabolic inhibitor of sulfation. Because MECA 79 stains HEV-like vessels at various sites of inflammation, recognition by L-selectin of ligands outside of secondary lymphoid organs may depend on sulfation. In addition to their reactivity with GlyCAM-1 and CD34, both MECA 79 and LEC-IgG recognize an independent molecule of similar 200 kD in a sulfate-dependent manner. Thus, this molecule, which we designate Sgp200, is an additional ligand for L-selectin.

2/7/12 (Item 2 from file: 72)

DIALOG(R) File 72:EMBASE

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8864828 EMBASE No: 93168582

Direct demonstration of heterogeneous, sulfated O-linked carbohydrate chains on an endothelial ligand for L-selectin

Imai Y.; Rosen S.D.

Department of Chemical Toxicology, University of Tokyo, Tokyo 113 Japan
GLYCOCONJUGATE J. (United Kingdom), 1993, 10/1 (34-39) CODEN: GLJOE

ISSN: 0282-0080 ADONIS ORDER NUMBER: 028200809300014Q

LANGUAGES: English SUMMARY LANGUAGES: English

We have previously identified endothelial ligands for L-selectin as sialylated, fucosylated and sulfated glycoproteins of approximately 50 kDa and 90 kDa (Sgp50 and Sgp90). In this report, we use the beta elimination reaction to demonstrate directly the presence of sulfated O-linked sugar chains on one of these ligands, after metabolic labeling with radiolabeled sulfate or fucose. All of the sulfated and the majority of the fucosylated O-linked sugar chains were shown to be sialylated by affinity chromatography on a Limax agglutinin column. Analyses by anion exchange and gel permeation chromatography revealed a complexity of sugar chains, which were heterogeneous both in charge and size. Charged groups other than sialic acid appeared to exert a predominant influence on the total charge of the sugar chains. The probable existence of a varying number of sulfate modifications per sugar chain is discussed.

2/7/13 (Item 3 from file: 72)

DIALOG(R) File 72:EMBASE

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7415800 EMBASE No: 89138243

Monoclonal anti-idiotypic antibody mimicking a tumor-associated sialoglycoprotein antigen induces humoral immune response against human small-cell lung carcinoma

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Division of Oncology, Department of Medicine, University Hospital of Zurich, CH-8091 Zurich Switzerland

INT. J. CANCER (USA), 1989, 43/5 (896-900) CODEN: IJCNA ISSN: 0020-7136

LANGUAGES: English

We have previously described the tumor-associated sialoglycoprotein antigen sGP90-135 defined by the murine LAM8 MAb. The antigen is characterized by strong membrane expression in a proportion of small-cell carcinomas of the lung, but little or no expression on normal tissues of

epithelial or neural origin or on blood cells. With the aim of obtaining anti-idiotypic antibodies which might be useful as surrogates for sGP90-135 in vaccination studies, LOU rats were immunized with LAM8 MAb and their spleen cells fused with Y3 rat myeloma cells. The LY8-229 hybrid was selected by an anti-idiotype competition radioimmunoassay on antigen-positive target cells. LY8-229 was shown to be a rat IgG1 with high specificity for LAM8 combining site. Solubilized small-cell carcinoma extract, as well as antibody SEN16, which recognizes the same tumor-associated antigen sGP90-135, selectively inhibited ^{125}I -LY8-229 binding to LAM8. Serum from BALB/c mice and DA rats immunized with anti-idiotypic antibody LY8-229 showed reactivity with antigen-positive target cell lines, but not with antigen-negative control cell lines. The induction of a specific immune response in 2 different species by the anti-idiotypic antibody LY8-229 suggests that LY8-229 bears the internal image of the antigen sGP90-135 and that it might be a candidate for immunotherapy trials in cancer patients.

2/7/14 (Item 1 from file: 154)

DIALOG(R) File 154: MEDLINE(R)

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09506704 96028304

Selective modulation of the expression of L-selectin ligands by an immune response.

Hoke D; Mebius RE; Dybdal N; Dowbenko D; Gribling P; Kyle C; Baumhueter S
; Watson SR

Department of Immunology, Genentech, South San Francisco, California
94080, USA.

Curr Biol (ENGLAND) Jun 1 1995, 5 (6) p670-8, ISSN 0960-9822

Journal Code: B44

Languages: ENGLISH

Document type: JOURNAL ARTICLE

BACKGROUND: The adhesion molecule L-selectin is expressed on the cell surface of lymphocytes and mediates their migration from the bloodstream into lymph nodes. L-selectin is able to recognize four glycoprotein ligands, three of which--Sgp50, Sgp90, and Sgp200--are sulphated, bind specifically to L-selectin and are synthesized by the high endothelial venules of the peripheral and mesenteric lymph nodes. One of these three sulphated L-selectin ligands, Sgp90, has been shown to be identical to the known surface marker CD34 and is expressed on the cell surface of endothelial cells. The cDNA encoding Sgp50 has been cloned, and its product, which has been designated GlyCAM-1, is secreted. The third ligand, Sgp200, is both secreted and cell-associated. We have investigated how the expression of these sulphated glycoproteins is regulated during an immune response. **RESULTS:** Here we demonstrated that, during a primary immune response, the expression and secretion of both GlyCAM-1 and Sgp200 are reduced, recovering to normal levels 7-10 days after antigen stimulation. In contrast, the expression of cell-associated CD34 and Sgp200 is relatively unaffected. These results may account for the modest decreases in the binding of an L-selectin-IgG fusion protein to high endothelial venules of inflamed peripheral lymph nodes that have been observed after antigen exposure. **In vivo** experiments show that, following the decrease in the levels of secreted GlyCAM-1 and Sgp200, migration of lymphocytes from the blood stream into lymph nodes remains L-selectin-dependent, but more lymphocytes home to antigen-primed than unprimed peripheral lymph nodes.

CONCLUSIONS: We suggest that the secreted forms of the L-selectin ligands GlyCAM-1 and Sgp200 act as modulators of cell adhesion, and that

cell-associated CD34 and Sgp200 are the ligands that mediate the initial loose binding of lymphocytes to high endothelial venules.

2/7/15 (Item 2 from file: 154)

DIALOG(R) File 154: MEDLINE(R)

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08749378 94064378

Robert Feulgen Lecture 1993. L-selectin and its biological ligands.
Rosen SD

Department of Anatomy, University of California, San Francisco
94143-0452.

Histochemistry (GERMANY) Sep 1993, 100 (3) p185-91, ISSN 0301-5564
Journal Code: G9K

Contract/Grant No.: GM23547, GM, NIGMS

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

This review considers the leukocyte adhesive receptor known as L-selectin. This protein, belonging to the selectin family of cell-cell adhesion receptors, mediates adhesion by virtue of a C-type lectin domain at its amino terminus. The protein was discovered as a lymphocyte homing receptor involved in the attachment of lymphocytes to high endothelial venules (HEV) of lymph nodes. Its widespread distribution on all leukocyte populations underlies a more general role in a variety of leukocyte-endothelial interactions. In the HEV interaction, cognate HEV ligands for L-selectin have been identified as two sulfated, sialylated, and fucosylated glycoproteins, known as GlyCAM-1 and Sgp90. These ligands have mucin-like domains which confer important properties for their proposed adhesive function. The carbohydrate features of these ligands, essential for their interaction with L-selectin, are reviewed. The existence of extralymphoid ligands for L-selectin is also discussed. (75 Refs.)

2/7/16 (Item 1 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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118076591 CA: 118(9)76591u PATENT

Assays for inhibitors of leukocyte adhesion

INVENTOR(AUTHOR): Rosen, Steven; Singer, Mark; Imai, Yasuyuki; Yednock,

Ted

LOCATION: USA

ASSIGNEE: University of California

PATENT: PCT International ; WO 9219761 A1 DATE: 921112

APPLICATION: WO 92US3606 (920501) *US 695805 (910506)

PAGES: 32 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12Q-001/00A;
G01N-033/53B DESIGNATED COUNTRIES: CA; JP DESIGNATED REGIONAL: AT; BE; CH
; DE; DK; ES; FR; GB; GR; IT; LU; MC; NL; SE

SECTION:

CA209002 Biochemical Methods

IDENTIFIERS: leukocyte adhesion inhibitor identification, selectin receptor cell adhesion inhibitor, lymphocyte homing receptor adhesion inhibitor

DESCRIPTORS:

Immunoglobulins...

chimeric mol. of lymphocyte homing receptor component and component of,

intercellular adhesion mediated by, inhibitors of, identification of Glycoproteins, biological studies...

extracellular region of, of endothelial cell, in selectin receptor-mediated intercellular adhesion inhibitor identification

Blood vessel, endothelium, composition...

extracellular region of surface glycoprotein of cells of, in selectin receptor-mediated intercellular adhesion inhibitor identification

Lymphocyte...

fluoresceinated receptor-binding agent and, in lymphocyte homing receptor-mediated intercellular adhesion inhibitor identification

Egg, jelly coat...

fucan of, lymphocyte homing receptor competitive binding of Cytometry, flow... Glycolipids, sulfo-... Polysaccharides, phosphates, esters ... Polysaccharides, sulfates, esters... Sulfatides... Sulfolipids, glyco-... in selectin receptor-mediated intercellular adhesion inhibitor identification

Glycoproteins, specific or class, selectins...

intercellular adhesion mediated by, inhibitors of, identification of Receptors...

lymphocyte homing, intercellular adhesion mediated by, inhibitors of, identification of

Adhesion, bio-...

selectin receptor-mediated, inhibitors of, identification of Sialoglycoproteins...

Sgp50, extracellular region of, of endothelial cell, in selectin receptor-mediated intercellular adhesion inhibitors identification Sialoglycoproteins...

Sgp90, extracellular region of, of endothelial cell, in selectin receptor-mediated intercellular adhesion inhibitors identification

Antibodies...

to receptor-binding agents, in lymphocyte homing receptor-mediated intercellular adhesion inhibitor identification

CAS REGISTRY NUMBERS:

9005-49-6 biological studies, lymphocyte homing receptor competitive binding of

9044-08-0 core, of Hansenula hostii, in selectin receptor-mediated intercellular adhesion inhibitor identification

9072-19-9D fluoresceinated, ELISA with, lymphocyte homing receptor-mediated intercellular adhesion inhibitor identification in relation to

9042-14-2 9072-19-9 in selectin receptor-mediated intercellular adhesion inhibitor identification

1256-86-6 12707-58-3 19553-76-5 19600-01-2 37758-47-7 54827-14-4

59247-13-1 62010-37-1 68652-37-9 85305-88-0 103370-52-1 lymphocyte homing receptor competitive binding of

64612-25-5 lymphocyte homing receptor competitive binding of, of egg jelly

2321-07-5D receptor binding agent conjugates, in selectin

receptor-mediated intercellular adhesion inhibitor identification

2/7/17 (Item 1 from file: 351)

DIALOG(R) File 351:DERWENT WPI

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009351757 WPI Acc No: 93-045231/05

XRAM Acc No: C93-020417

XRPX Acc No: N93-034678

Use of a blocking agent which inhibits leukocyte homing receptor

mediated binding - for treating, diagnosing and monitoring e.g.
multiple sclerosis

Patent Assignee: (REGC) UNIV CALIFORNIA

Author (Inventor): GEOFFROY J; HUANG K; ROSEN S; SINGER M; GEOFFREY J

Number of Patents: 004

Number of Countries: 017

Patent Family:

CC Number	Kind	Date	Week	
WO 9300919	A1	930121	9305	(Basic)
US 5227369	A	930713	9329	
EP 593658	A1	940427	9417	
JP 7505859	W	950629	9534	

Priority Data (CC No Date): US 727280 (910711)

Applications (CC, No, Date): WO 92US5836 (920713); JP 93501815 (920713); WO 92US5836 (920713); EP 92915758 (920713); WO 92US5836 (920713)

Language: English

EP and/or WO Cited Patents: 21Jnl.Ref; EP 153875; EP 184040; US 4294818; US 4618601; US 4752563; US 4818686; US 4839276; US 4935343; US 4948726; US 4994466; US 5036102; US 5089479

Designated States

(National): JP

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; MC; NL; SE; LI

Filing Details: JP07505859 Based on WO 9300919; EP0593658 Based on WO 9300919

Abstract (Basic): WO 9300919 A

Treating a demyelinating disease in a patient is claimed, comprising administering a compsn. comprising a carrier and a blocking agent which inhibits lymphocyte homing receptor (LHR)-mediated binding of leukocytes to myelin, the blocking agent being present in an amt. to inhibit LHR-mediated adhesion. The blocking agent may be e.g. mannose-6-phosphate, fructose-1-phosphate, a fragment of fucoidin or the phosphomannan monoester core from Hansenula hostii (PPME), Sgp50, Sgp90, an immunoglobulin or an isolated LHR.

Also claimed is a method of blocking LHR-mediated adhesion of leukocytes to myelin in a patient, comprising administering a compsn. comprising a carrier and a blocking agent which inhibits LHR-mediated binding.

USE - The blocking agents selectively bind either LHR or the recognition determinant on myelin. They can be used in the diagnosis and treatment of demyelinating diseases such as multiple sclerosis (MS), acute disseminated encephalomyelitis, acute necrotising haemorrhagic encephalomyelitis and HIV associated myopathy. Dwg.0/0

Abstract (US): 9329 US 5227369 A

Treating the demyelinating effect comprises admin. of a compsn. comprising a protein blocking agent which inhibits LHR-mediated binding of leukocytes to myelin and inhibits adhesion. Blocking agent comprises an extracellular region of an endothelial cell surface glycoprotein or an immunoglobulin.

USE/ADVANTAGE - Used for treating and diagnosing demyelinating disease e.g. multiple sclerosis. Dwg.0/0

Derwent Class: B05; S03;

Int Pat Class: A61K-031/70; A61K-031/715; A61K-037/02; A61K-038/00; A61K-039/395; A61K-045/00; G01N-033/53

009271472 WPI Acc No: 92-398884/48

Related WPI Accession(s): 92-398862

XRAM Acc No: C92-177007

Inhibitors of inter-cellular adhesion mediated by selectin receptor - are isolated by using assays with the receptor and receptor-binding agent

Patent Assignee: (GETH) GENENTECH INC; (REGC) UNIV CALIFORNIA

Author (Inventor): IMAI Y; LASKY L A; ROSEN S D; SINGER M S; ROSEN S; SINGER M; YEDNOCK T

Number of Patents: 003

Number of Countries: 017

Patent Family:

CC Number	Kind	Date	Week	
WO 9219761	A1	921112	9248	(Basic)
EP 584194	A1	940302	9409	
EP 584194	A4	940928	9534	

Priority Data (CC No Date): US 695805 (910506)

Applications (CC, No, Date): EP 92911137 (); WO 92US3606 (920501); EP 92911137 (920501); WO 92US3606 (920501)

Language: English

EP and/or WO Cited Patents: 3.Jnl.Ref; WO 9013300 X

Designated States

(National): CA; JP

(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; MC; NL; SE; LI

Filing Details: EP0584194 Based on WO 9219761

Abstract (Basic): WO 9219761 A

A method for assaying a test cpd. for the ability to inhibit intercellular adhesion mediated by a selectin receptor, comprising (a) contacting the test cpd. with the receptor and an isolated receptor-binding agent (RBA) selected from a phosphorylated polysaccharide, a sulphated polysaccharide and a cpd. comprising the extracellular region of an endothelial cell surface glycoprotein and (b) detecting the ability of the test cpd. to inhibit binding between the receptor and the agent.

The receptor may be a lymphocyte homing receptor or a chimeric molecule comprising a lymphocyte homing receptor component and an immunoglobulin component. The RBA may be e.g. PPME, fucoidin, dextran sulphate, Sgp50 or Sgp90. The RBA is pref. labelled with fluorescein.

USE/ADVANTAGE - The assays allow large scale in vitro screening of a variety of cpds. The inhibitors obtd. can be used for treating selectin-mediated disease responses, e.g. inflammation, rheumatoid arthritis, post-ischemic leukocyte-mediated tissue damage, frost-bite injury or shock, adult respiratory distress syndrome, asthma, traumatic shock, septic shock, atopic dermatitis, psoriasis, inflammatory bowel disease, atherosclerosis or clotting. They can also be used for inhibiting or preventing tumour metastasis in e.g. colon carcinoma and melanoma. The inhibitors can also be used to target other pharmaceutical cpds. such as anti-inflammatory agents or antioxidants to the sites of injury. Dwg.0/0

Derwent Class: B04; D16;

Int Pat Class: A61K-037/02; C07K-013/00; C12N-005/10; C12N-015/12; C12N-015/13; C12N-015/62; C12P-021/02; C12P-021/08; C12Q-001/00; G01N-033/53

?s sgp90 and cd334

41 SGP90
0 CD334
S3 0 SGP90 AND CD334
?s sgp90 and cd334

41 SGP90
8094 CD34
S4 12 SGP90 AND CD34
?rd s4

>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records

S5 6 RD S4 (unique items)
?t s5/7/all

5/7/1 (Item 1 from file: 55)
DIALOG(R) File 55:BIOSIS PREVIEWS(R)
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11473588 BIOSIS Number: 98073588

Localization of ligands for L-selectin in mouse peripheral lymph node
high endothelial cells by colloidal gold conjugates

Kikuta A; Rosen S D

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Japan

Blood 84 (11). 1994. 3766-3775.

Full Journal Title: Blood

ISSN: 0006-4971

Language: ENGLISH

Print Number: Biological Abstracts Vol. 099 Iss. 004 Ref. 043998

L-selectin, a Ca-2+-dependent lectin-like receptor, mediates lymphocyte attachment to high endothelial venules (HEV) of peripheral lymph nodes (PLN) during the process of lymphocyte homing. Two endothelial-derived ligands for L-selectin, known as GlyCAM-1 (Sgp50) and CD34 (Sgp90), have been identified by affinity precipitation of lymph node extracts with a chimeric molecule that combines the extracellular domains of L-selectin with the human IgG1 Fc region (L-selectin-IgG) (J Cell Biol 110:2221, 1990). Here, using a histologic probe based on colloidal gold conjugated to L-selectin-IgG (LS-IgG), we performed morphologic mapping of the HEV ligands in PLN at both the light and electron microscopic levels. With a postembedding labeling method, intense LS-Ig-gold staining of PLN HEV was observed, while the HEV of Peyer's patches (PP) were negative. The specificity of LS-Ig-gold staining was established by pretreatment of sections with sialidase and coincubation of sections with EGTA, fucoidin, or L-selectin-IgG itself. In ultrastructural studies of high endothelial cells (HEC), gold particles were bound to the trans-Golgi network (TGN) and to peripheral vesicles in the cytoplasm. Gold labeling was also detected in a patchy distribution on the entire luminal vascular surface of HEC. Although the perivascular fibroreticular sheath of HEV was frequently labeled, limited labeling was observed on the basolateral surfaces of the HEC. In most cases, the HEC membrane surrounding migrating lymphocytes was negative. These results show that L-selectin ligands pass through the Golgi apparatus during their biosynthesis, are stored in secretory granules, and are expressed on the vascular luminal surface of the HEC. A polyclonal

endothelium are involved in the migration of lymphocytes through peripheral lymph nodes and of neutrophils to sites of inflammation. A recombinant L-selectin stains high endothelial venules (HEVs) in lymph nodes and recognizes sulfated carbohydrates found on two endothelial glycoproteins, Sgp50 and Sgp90. Amino acid sequencing of purified Sgp90 revealed a protein core identical to that of CD34, a sialomucin expressed on hematopoietic stem cells and endothelium. A polyclonal antiserum to recombinant murine CD34 stains peripheral lymph node endothelium and recognizes Sgp90 that is functionally bound by L-selectin. Thus, an HEV glycoform of CD34 can function as a ligand for L-selectin.

5/7/4 (Item 1 from file: 72)
DIALOG(R) File 72:EMBASE
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9406303 EMBASE No: 94357259

Sulfation-dependent recognition of high endothelial venules (HEV)-ligands by L-selectin and MECA 79, an adhesion-blocking monoclonal antibody
Hemmerich S.; Butcher E.C.; Rosen S.D.

Department of Anatomy, University of California, San Francisco, CA
94143-0452 USA

J. EXP. MED. (USA), 1994, 180/6 (2219-2226) CODEN: JEMEA ISSN:
0022-1007

LANGUAGES: English SUMMARY LANGUAGES: English

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5/7/5 (Item 1 from file: 154)
DIALOG(R) File 154: MEDLINE(R)
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09506704 96028304

Selective modulation of the expression of L-selectin ligands by an immune response.

Hoke D; Mebius RE; Dybdal N; Dowbenko D; Gribling P; Kyle C; Baumhueter S;
Watson SR

Department of Immunology, Genentech, South San Francisco, California

94080, USA.

Curr Biol (ENGLAND) Jun 1 1995, 5 (6) p670-8, ISSN 0960-9822

Journal Code: B44

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BACKGROUND: The adhesion molecule L-selectin is expressed on the cell surface of lymphocytes and mediates their migration from the bloodstream into lymph nodes. L-selectin is able to recognize four glycoprotein ligands, three of which--Sgp50, Sgp90, and Sgp200--are sulphated, bind specifically to L-selectin and are synthesized by the high endothelial venules of the peripheral and mesenteric lymph nodes. One of these three sulphated L-selectin ligands, Sgp90, has been shown to be identical to the known surface marker CD34 and is expressed on the cell surface of endothelial cells. The cDNA encoding Sgp50 has been cloned, and its product, which has been designated GlyCAM-1, is secreted. The third ligand, Sgp200, is both secreted and cell-associated. We have investigated how the expression of these sulphated glycoproteins is regulated during an immune response. **RESULTS:** Here we demonstrated that, during a primary immune response, the expression and secretion of both GlyCAM-1 and Sgp200 are reduced, recovering to normal levels 7-10 days after antigen stimulation. In contrast, the expression of cell-associated CD34 and Sgp200 is relatively unaffected. These results may account for the modest decreases in the binding of an L-selectin-IgG fusion protein to high endothelial venules of inflamed peripheral lymph nodes that have been observed after antigen exposure. **In vivo** experiments show that, following the decrease in the levels of secreted GlyCAM-1 and Sgp200, migration of lymphocytes from the blood stream into lymph nodes remains L-selectin-dependent, but more lymphocytes home to antigen-primed than unprimed peripheral lymph nodes. **CONCLUSIONS:** We suggest that the secreted forms of the L-selectin ligands GlyCAM-1 and Sgp200 act as modulators of cell adhesion, and that cell-associated CD34 and Sgp200 are the ligands that mediate the initial loose binding of lymphocytes to high endothelial venules.

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This review considers the leukocyte adhesive receptor known as L-selectin. This protein, belonging to the selectin family of cell-cell adhesion receptors, mediates adhesion by virtue of a C-type lectin domain at its amino terminus. The protein was discovered as a lymphocyte homing receptor involved in the attachment of lymphocytes to high endothelial venules (HEV) of lymph nodes. Its widespread distribution on all leukocyte populations underlies a more general role in a variety of leukocyte-endothelial interactions. In the HEV interaction, cognate HEV ligands for L-selectin have been identified as two sulfated, sialylated, and fucosylated glycoproteins, known as GlyCAM-1 and Sgp90. These ligands

have mucin-like domains which confer important properties for their proposed adhesive function. The carbohydrate features of these ligands, essential for their interaction with L-selectin, are reviewed. The existence of extralymphoid ligands for L-selectin is also discussed. (75 Refs.)